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Review Article

Bacteriotherapy: A Strategic Update for Oral Physicians.

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Abstract:

As we know, there is a lot of information now in the public domain on the use of probiotics to gain a beneficial effect within the digestive tract. In recent years, there has been a lot of interest in the use of probiotics in maintaining good oral health and treating oral infections. Evidence now suggests that probiotics may function not only by direct inhibition of, or enhanced competition with, pathogenic micro-organisms, but also by more subtle mechanisms including modulation of the mucosal immune system. Similarly, prebiotics could promote the growth of beneficial micro-organisms that comprise part of the resident microbiota. A complete understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics will be essential to assess their long-term consequences for oral health and disease. This paper will review the data on the use of probiotics for oral care or disease prevention, and discuss some of the issues that arise from their use, as well as identify questions that still need to be answered.

Key words: Prebiotics, Probiotics, Bacteriotherapy, Periodontal diseases, Dental caries.

Introduction

In recent years, there have been significant changes with respect to the effectiveness of, and attitudes towards, conventional antimicrobial therapy to combat disease. The age-old quote by Hippocrates, 'Let food be thy medicine and medicine be thy food', is certainly the tenet of today. The market for functional foods that promote health beyond providing basic nutrition, is flourishing. Within the functional foods, is the small but rapidly expanding arena of probiotics. The use of probiotics in antibiotic resistance is termed microbial interference therapy (replacement therapy or Bacteriotherapy). With increasing understanding that beneficial microbes are required for health, probiotics may become a common therapeutic tool used by health care practitioners in the not-too-distant future. There is a long tradition, particularly in parts of Europe and Asia, of ingesting microbes or food products that affect the intestinal microbiota in ways that are believed to provide beneficial health effects, i.e. intake of probiotics and prebiotics. A complete

understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics will be essential to assess their long-term consequences for oral health and disease.[1-4]

What Are Probiotics, Prebiotics And Synbiotics:

The term probiotic, meaning "for life," is derived from the Greek language. According to a WHO/ FAO report (2002), probiotics are 'Live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host'. International Life Science Institute (ILSI) Europe suggests a definition according to which a probiotic is 'a live microbial food ingredient that, when ingested in sufficient quantities, exerts health benefits on the consumer'. Both definitions have in common the idea that probiotic micro-organisms are living and exert proven health effects. Prebiotic is a non-digestible food ingredient that confers benefits on the host by selectively stimulating the growth and/or activity of one bacterium or a group of bacteria in the colon, and thus improve the host health. Prebiotics are dietary carbohydrates that escape digestion in the upper gastrointestinal tract, alter the bacterial composition of the gut, by changing the type of the substrate provided to the existing microbial population in the gut e.g. fructo oligosaccharides, gluco-oligosaccharides and inulin. The term synbiotic is used when a product contains both probiotics and prebiotics. Because the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound.[1-5]

Mechanisms of Action of Probiotics in General and Specifically On Oral Health:

The mechanisms by which probiotics exert their effects are largely unknown, but may involve modifying gut pH, antagonizing pathogens through production of antimicrobial compounds, competing for pathogen binding and receptor sites as well as for available nutrients and growth factors, stimulating immunomodulatory cells, and producing lactase. Probiotic bacteria have been shown to influence the immune system through several molecular mechanisms.[1]

Characteristics of Good Probiotics:

Fuller in 1989 listed the following as features of a good probiotic: It should be a strain, which is capable of exerting a beneficial effect on the host animal, e.g. increased growth or resistance to disease. It should be non-pathogenic and non-toxic and should be present as viable cells, preferably in large numbers. It should be capable of surviving and metabolising in the gut environment e.g. resistance to low pH and organic acids. It should be stable and capable of remaining viable for periods under storage and field conditions. The characteristic features of ideal prebiotics are as follows: They are neither to be hydrolysed nor absorbed by mammalian enzymes or tissues. They are selectively enriched with a limited number of beneficial bacteria. The most important characteristic feature is that prebiotics can alter the intestinal micro-flora and its activities. Prebiotics can also change luminal or systemic aspects of the host defense system.[6-16]

Examples of Prebiotics and Probiotics:

There are a number of different organisms that can be classified as "probiotics". The most common probiotic strains belong to the genera Lactobacillus and Bifidobacterium. *Lactobacillus* species from which probiotic strains have been isolated include *L. acidophilus, L. johnsonii, L. casei, L. rhamnosus, L. gasseri,* and *L. reuteri. Bifidobacterium strains* include *B. bifidum, B. longum,* and *B. infantis*. Some of the commonly known prebiotics are Lactose, Inulin, Fructo oligosacccharides, Galacto oligosaccharides and Xylo oligosaccharides. Prebiotics are naturally found plenty in certain fruits like bananas, asparagus, garlic, tomato and onion wheat.

Synergism of Prebiotics and Probiotics:

Prebiotics when combined with probiotics have many advantages. Basically, prebiotics selectively stimulate the growth of probiotics, which is dose and strain dependent. Prebiotics serve as a selective growth substrate for the probiotics strain during fermentation, during the period of storage, or during its passage through the gut. These two

combinations implant live microbial dietary supplements and create a congenial environment for their survival in gut flora. Thereby, this environment in gut flora improves healthy microbial balance. So, the combination of prebiotics and probiotics may have additive and synergistic effect in providing better oral health conditions.[17-20]

Probiotics and General Health:

Probiotics have traditionally been used to treat diseases related to the gastrointestinal tract. Studies suggest that probiotics may be useful in treatment of patients with hypertension, urogenital infections, lactose intolerance, and elevated levels of cholesterol. Other areas of application include probiotic effects against *Helicobacter pylori* infections in the stomach, alcoholic liver disease, small bowel bacterial overgrowth, ulcerative colitis, allergy to milk protein, juvenile chronic arthritis, anti-oxidative effects, asthma, hepatic encephalopathy and their use as vaccine delivery vehicles.[13,16]

Role of Bacteriotherapy in Dental caries:

In caries, there is an increase in acidogenic and acidtolerating species such as mutans streptococci and lactobacilli, although other bacteria with similar properties can also be found like *Bifidobacteria, nonmutans streptococci*, A*ctinomyces spp., Propionibacterium spp., Veillonella spp. and Atopobium spp.* Use of probiotics and molecular genetics to replace and displace cariogenic bacteria with noncariogenic bacteria has shown promising results. These studies have employed different approaches:[1,3]

- Early studies concentrated on utilising bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances (BLIS) that specifically prevented the growth of cariogenic bacteria.
- One approach has been to identify food grade and probiotic bacteria which have ability to colonize teeth and influence the supragingival plaque.
- Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.
- Another approach utilised recombinant strain of S. mutans expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.
- Similarly, genetically modified probiotics with enhanced properties can be developed ('designer probiotics'). For example, a recombinant strain of Lactobacillus that expressed antibodies targeting one of the major adhesions of S. mutans (antigen I/ II) was able to reduce both the viable counts of S. mutans and the caries score in a rat model.

Comelli EM et al (2002) studied 23 dairy bacterial strains for the prevention of dental caries and reported that only two strains namely Streptococcus thermophilus and Lactcoccus lactis were able to adhere to saliva-coated hydroxyapatite and were further successfully incorporated into a biofilm similar to the dental plaque. Furthermore, they could grow together with five strains of oral bacterial species commonly found in supragingival plaque. In this system, Lactococcus lactis was able to modulate the growth of the oral bacteria, and in particular to diminish the colonization of Streptococcus oralis, Veillonella dispar, Actinomyces naeslundii and of the cariogenic Strep.sobrinus.[1,3]

Bacteriotherapy in Prevention of Periodontal Diseases:

Patients with moderate to severe gingivitis who were given either one of two L. reuteri formulations had reduced plaque and gingivitis scores compared to a placebo group. Similarly, the regular (three times daily for eight weeks) intake of tablets containing Lactobacillus salivarius resulted in benefits in terms of pocket probing depth and plaque index in individuals at high risk of periodontal disease (smokers) compared to a placebo control group. Other studies have aimed to identify organisms that have the potential for probiotic action that may protect against periodontal diseases. The subgingival application of beneficial oral bacteria (e.g. Streptococcus sanguinis, Streptococcus salivarius and S. mitis) (replacement therapy) has been shown to delay recolonisation by periodontal pathogens, reduce inflammation, and improve bone density and bone levels in a beagle dog model. Koll-

Klais et al. observed that Lactobacillus gasseri strains isolated from periodontally healthy subjects were more efficient at inhibiting the growth of A. actinomycetemcomitans than strains from periodontally diseased subjects, and also inhibited the growth of P. gingivalis and P. intermedia; this correlated with an inverse relationship between carriage of homofermentative lactobacilli and subgingival colonisation by A. actinomycetemcomitans, P. gingivalis and P. intermedia.

The mechanisms of inhibition of periodontal pathogens have not been fully clarified. The inhibitory activity displayed by homofermentative lactobacilli against periodontal pathogens was principally related to their production of acid, not to H_2O_2 or bacteriocin production. Hojo et al. suggested that bifidobacteria inhibit some black pigmented anaerobes by competing for an essential growth factor, vitamin K, although there was no significant relationship between higher bifidobacterial counts and lower black-pigmented anaerobe counts. Recently, a bacteriocin purified from *Lactobacillus casei* killed *P. gingivalis* but its use was proposed as a novel chemotherapeutic agent rather than as strain development for probiotic applications.[4,8,11,12,20]

Bacteriotherapy and Imbalanced Oral Ecosystem:

Halitosis, the oral malodor, is a condition normally ascribed to disturbed commensal microflora equilibrium. In oral malodor, the sulphur containing gases (hydrogen sulfide, methyl mercaptan and dimethyl sulfide), which are derived from the bacterial degradation of sulphur containing amino acids in the oropharynx, play a significant role. A diverse consortium of bacteria has been found to contribute to the problem, including *Fusobacterium nucleatum, P. gingivalis, P. intermedia* and Treponema denticola. Other gases, such as indole, skatole, putrescine, cadaverine and acetone, are also relevant and sometimes even the dominant cause of halitosis, although their substantively is much lower. Given that oral microorganisms, especially those on the tongue, are the primary cause of halitosis, current treatments focus on the use of chemical or physical antibacterial regimes to reduce the numbers of these bacteria. Kang et al (2006) have shown a definite inhibitory effect on the production of volatile sulfur compounds (VSC) by *F. nucleatum* after ingestion of *Weissella cibaria* both in vitro and in vivo. In children, a marked reduction in the levels of H2S and CH3SH by approximately 48.2% ($P < 0.01$) and 59.4% ($P < 0.05$), respectively, was registered after gargling with *W. cibaria* containing rinse. The possible mechanism in the VSC reduction is the hydrogen peroxide generated by *W. cibaria* that inhibits the proliferation of *F. nucleatum*. *Streptococcus salivarius*, also a possible candidate for an oral probiotic, has demonstrated inhibitory effect on VSC by competing for colonization sites with species causing an increase in levels of VSC.[10,16,17]

Bacteriotherapy and Candidiasis:

Candida albicans is among the most common infectious agents in the oral cavity. The incidence of yeast infections is higher at older age and under conditions of impaired immunity. Hatakka et al were the first to perform a randomized, double-blind, placebo-controlled study on the effect of probiotics on the prevalence of oral candida. A decrease in the prevalence of C. albicans in the elderly after consumption of probiotic cheese containing *L. rhamnosus* GG and *Propionibacterium freudenreichii ssp*. shermanii JS which was as an interesting observation in this randomized placebo-controlled trial. A concomitant feature of the probiotic activity observed in this study was the diminished risk of hyposalivation and the feeling of dry mouth of the subjects. It could be hypothesized that extending research on oral pathology, such as yeast infections, with respect to probiotics, and analyzing the molecular mechanisms of probiotic activity, might further broaden the field of their potential applications.[6,17]

Bacteriotherapy in India:

In India, Sporolac, Saccharomyces boulardii and yogurt (L. bulgaricus + L. thermophillus) are the most common ones used. Sporolac is manufactured using Sporolactobacilli. Lactobacilli solution is an example of a probiotic, usually given to pediatric patients. The latest and recent addition to the list of probiotics in India is made up of genetically modified *Bacillus mesentricus* which act as an alternate to B-complex

capsules. Only sporulating lactobacilli are used with some of the antibiotic preparations.[18]

Safety Issues and Potential Risks:

The issue of protection is of particular concern during the past few years due to the amplified probiotic supplementation of different food products. The increased probiotic utilization inevitably leads to increased concentrations of these species in the host organism. Lactobacillus bacteremia is a rare entity, and data on its clinical significance are mainly found through case reports. There have been some cases of bacteraemia and fungaemia associated with probiotic use, although these have been in subjects who are immunocompromised or who suffer from chronic disease or short gut syndrome. Other predisposing factors include prior prolonged hospitalization and prior surgical intervention. An individual who had been taking L. rhamnosus in a probiotic preparation developed Lactobacillus endocarditis following dental treatment.

The species that most commonly exhibit probiotic benefits are lactobacilli and other lactic acid bacteria, and the production of acid is often thought to be an important component of their protection against pathogenic colonisation. However, Lactobacillus spp. and acid production by acidogenic plaque populations play a significant part in the development of caries. It is clear that careful selection of the strain to be ingested for a particular disease is essential and the mode and timing of administration can be crucial, as well as the age and health of the individual taking the probiotic.[2,4,9,14,17]

Future Trends of Bacteriotherapy:

In field of oral immunology, probiotics are being used as passive local immunization vehicles against dental caries. Recently, by means of systemic immunization with a multivalent vaccine, *L. rhamnosus* GG was chosen as the vehicle to harbor IgG because of its widely known health benefits in humans and animals. High titers of antibodies against human cariogenic bacteria, *S. mutans* and *S. sobrinus*, were produced in bovine colostrums by a vehicle of fermented milk. It was found that early mucosal colonization with *E. coli* bacteria stimulates the mucosal immune system to produce specific antibodies as well as non-specific secretory immunoglobulins.

In oncology field, serious systemic infections may occur during cancer chemotherapy because of disturbances in the oropharyngeal and gastrointestinal microflora, impaired mucosal barrier functions and immunosuppression. Regarding the present condition treatment with probiotics "L. plantarum 299v" improves food intake and body weight in chemotherapized animals. Chosen probiotic strain reinforces the oral cavity, along with the gastrointestinal tract, as a source for bacterial dissemination. The capacity to assess the gut microbiota has expanded dramatically with the advent of molecular techniques. Real-time quantitative polymerase chain reaction procedures are among the promising tools for studies on intestinal microbiota composition.

In the present day technology has improved drastically. NASA of USA is carrying out research to develop probiotic products which enable humans live in space. For all these valid reasons, the use of probiotics has become an emerging subject in the field of dentistry at present. Probiotics combined with prebiotics are innovative and revolutionary method in the treatment of dental diseases. [5,15,17]

Conclusion:

The use of probiotics for use in oral care applications is gaining momentum. There is increasing evidence that the use of existing probiotic strains can deliver oral health benefits. Further work will be needed to fully optimize and quantify the extent of this benefit. However, whether considering probiotics or prebiotics, it will be essential to develop an understanding of the broad ecological changes induced in the mouth by their ingestion and the long-term consequences of their use on oral health and disease. Further studies on the combined effect of different probiotics & prebiotics should be carried out in order to authenticate the possible additive, cumulative, or competitive modes of action in the oral environment.

In addition, variation in the dosage for different preventive or therapeutic purposes are also to be studied carefully in order to

avoid ill-effects of the species that ferment sugar and lower oral pH that are detrimental to the teeth. Apart from this, general safety aspects such as those related to potential invasiveness and antibiotic resistance genes must be screened. In conclusion, probiotics have made their way into oral healthcare and are more likely to be our friend than our enemy. Despite our rapidly increasing knowledge of pathogen–host interactions, the role of beneficial bacteria in preventing the emergence of pathogenic species and oral health remains obscure. There is a great need to elucidate the role of the oral beneficial microbiota, to identify beneficial bacteria and to conduct proper large-scale studies on the usefulness of probiotics to maintain or improve oral health.

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